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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,646	03/24/2005	Takaaki Terahara	28363U	8337

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THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314

EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
12/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,646	TERAHARA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 07/17/09 are acknowledged.

2. Claims 2, 5, and 7 were cancelled.

3. Claims 1, 4, and 6 were amended.

4. Claims 1, 3-4, and 6 are included in the prosecution.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3-4, and 6 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Miranda et al. (US 5,656,286), in view of Hoffman (US 5,820,876).

Miranda teaches "a transdermal drug delivery composition wherein a blend of polymers is utilized to affect the rate of drug delivery from the composition. More specifically, a plurality of polymers … having differing solubility parameters, preferably immiscible with each other, adjusts the solubility of the drug in a polymeric adhesive system formed by the blend, affects the maximum concentration of the drug in the system, and modulates the delivery of the drug from the composition and through the

dermis" (Col. 1, lines 24-34). Styrene-isoprene-styrene block copolymers are disclosed as rubber-based pressure-sensitive adhesives useful in the transdermal composition (Col. 11, lines 20-24). Acrylate polymers useful in the composition are "polymers of one or more monomers of acrylic acids and other copolymerizable monomers … the acrylate polymer is composed of at least 50% by weight of an acrylate or alkyl acrylate monomer, from 0 to 20% of a functional monomer copolymerizable with the acrylate, and from 0 to 40% of other monomers … Acrylate monomers which can be used include … butyl methacrylate, … 2-ethylhexyl acrylate, …" (Col. 10, lines 46-62). Functional monomers that are copolymerizable with the alkyl acrylates include methacrylic acid, dimethylaminoethyl methacrylate (Col. 10, line 66 to Col. 11, line 4). The antiparkinsonian drug, pergolide, is disclosed as a drug that can be administered by the transdermal drug delivery system (Col. 23, lines 45-49).

Miranda does not expressly teach 2-ethylhexyl acrylate-vinyl acetate copolymer.

Hoffman teaches a transdermal therapeutic system for supplying active substances to the skin (Abstract). The active substance reservoir matrix can be a rubber material such as styrene-isoprene-styrene block copolymer (Col. 4, lines 2-6). Adhesive materials including a self-crosslinking acrylate copolymer, e.g. of 2-ethyl-hexyl acrylate, vinyl acetate and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM) are disclosed (Col. 7, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a transdermal drug delivery composition with styrene-isoprene-styrene block copolymers as rubber-based pressure-sensitive adhesives and

butyl methacrylate that is copolymerizable with methacrylic acid and dimethylaminoethyl methacrylate as suggested by Miranda, combine it with the transdermal composition with styrene-isoprene-styrene block copolymer, copolymer of 2-ethyl-hexyl acrylate and vinyl acetate, and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM), as suggested by Hoffman, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Hoffman teaches that the copolymer of 2-ethyl-hexyl acrylate and vinyl acetate is a self-crosslinking acrylate copolymer (Col. 7, lines 1-3).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of the styrene-isoprene-styrene block copolymer would have been obvious over the styrene-isoprene-styrene block copolymers taught by Miranda (Col. 11, lines 20-24). The limitation of 2-ethylhexyl acrylate-vinyl acetate copolymer would have been obvious over the copolymer of 2-ethyl-hexyl acrylate, vinyl acetate taught by Hoffman (Col. 7, lines 1-3). The limitation of the basic nitrogen including polymer would have been obvious over the acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM) taught by Hoffman (Col. 7, lines 1-8). The limitation of the weight ratio of the

content of the styrene-isoprene-styrene block copolymer to the content of the 2-ethyl-hexyl acrylate vinyl acetate copolymer would have been obvious over the teaching by Miranda that "by varying the amount of each type of monomer added, the cohesive properties of the resulting acrylate polymer can be changed as is known in the art" (Col. 10, lines 51-54). Therefore, one with ordinary skill in the art would modify the ratio of the styrene-isoprene-styrene block copolymer to the content of the 2-ethyl-hexyl acrylate vinyl acetate copolymer during the process of routine experimentation, and the recited ratio would have been an obvious variant unless there is evidence of criticality or unexpected results. The limitation of the adhesive layer further comprising an organic acid would have been obvious over the enhancers including ascorbic acid taught by Miranda (Col. 33, lines 16-34).

Regarding instant claims 3-4, the limitation of the drug would have been obvious over the pergolide taught by Miranda (Col. 11, lines 20-24)

Regarding instant claim 6, the limitation of the adhesive layer further comprising an alicyclic saturated hydrocarbon-based tackifier would have been obvious over the plasticizer or tackifying agents including aromatic hydrocarbons taught by Miranda (Col. 33, lines 37-45).

Response to Arguments

7. Applicant's arguments, see Page 4, filed 07/17/09, with respect to the rejection of claims 1 and 3-7 under 35 U.S.C. 103(a) as being unpatentable over Miranda et al. (US

5,656,286) in view of Hoffman (US 5,820,876) have been fully considered but are not persuasive.

Applicant argues that the data shown in Tables 1-4 on pages 34-37 of the present specification demonstrates the unexpectedly superior results achieved by the presently claimed patch formulations as compared to patch formulations lacking one or more of the copolymers recited in the presently pending claims, and therefore, the present claims are non-obvious over the applied references. Applicants argue that neither the Miranda et al. nor the Hoffmann references, taken alone or in combination, disclose all of the limitations of the presently pending claims, as required by *In re Wilson*.

This is not persuasive because one of ordinary skill in the art would have found it obvious to combine the styrene-isoprene-styrene block copolymers as rubber-based pressure-sensitive adhesives and butyl methacrylate is copolymerizable with methacrylic acid and dimethylaminoethyl methacrylate as suggested by Miranda, with the styrene-isoprene-styrene (SIS) block copolymer, the copolymer of 2-ethyl-hexyl acrylate (2-EHA) and vinyl acetate (VA), and the acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM), as suggested by Hoffman, and produce the instant invention. Based on the teaching of Miranda, one of ordinary skill in the art would know that the SIS block copolymer and the copolymer of 2-EHA and VA are used for adhesive or cohesive effect. Based on the teaching of Hoffman, one of ordinary skill in the art would know that the copolymer of 2-ethyl-hexyl acrylate (2-EHA) and vinyl acetate (VA), and the acrylic

resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM) are also used for adhesive or cohesive effect.

Both prior art references teach polymers for the same purpose, i.e., adhesion and cohesion. If one of ordinary skill in the art uses the polymers of each reference singly, the amount of the polymers would be higher to get the same adhesive or cohesive effect. When combining the polymers of the two references, one of ordinary skill in the art will not use the same (high) ratio he/she used when using the polymers of just one reference, i.e. one of ordinary skill in the art would adjust the amount of the polymers in order to achieve the desired adhesive/cohesive effect. It would be well within the scope of routine optimization, when the polymers of Miranda and Hoffman are combined, to modify and adjust the ratio of the polymers (SIS and 2-EHA-VA). The data in Tables 1-4 on pages 34-37 have been fully considered but is not unexpected or surprising in light of the combination of Miranda and Hoffman and the expected routine optimization following the combination.

The weight ratio of the content of the SIS block copolymer to 2-EHA-VA copolymer is a result effective variable that can be optimized to achieve the desired adhesion. The workable ranges or the ratio that achieve the recognized result (adhesion) may be optimized during routine experimentation. Please see MPEP 2144.05 and *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Applicant argues that the Hoffman reference does not describe the combination of components in a single layer of the embodied patch formulations as required by the presently pending claim 1 and that the Hoffman reference fails to describe the specific

layer structure of the patch formulations as recited in presently pending claim 1. Applicant argues that the Hoffman reference teaches away because Hoffman requires patch formulations where the layer structure and the combination of components in the layer(s) are different from those recited in the presently pending claims.

This is not persuasive because based on the teaching of Hoffman, one of ordinary skill in the art would know that the copolymer of 2-ethyl-hexyl acrylate (2-EHA) and vinyl acetate (VA), and the acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from RÖHM) are also used for adhesive or cohesive effect. One of ordinary skill in the art would find it obvious to include a copolymer of 2-ethyl-hexyl acrylate and vinyl acetate as an adhesive in patch formulations with a reasonable expectation of success in producing a functional cohesive patch formulation, thereby rendering instant claims obvious.

Applicant argues that neither the Miranda et al. nor the Hoffman references, either taken alone or in combination, describe the inclusion of an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid in their respective patch formulations.

This is not persuasive because the enhancers including ascorbic acid as taught by Miranda (Col. 33, lines 16-34) render the organic acid limitation of amended claim 1 obvious.

Applicants argue that there is no suggestion in the art to modify the combination of references to achieve the patch formulation of the presently pending claims with the specific components in their recited ratio and that accordingly, a prima facie case of

obviousness has not been established. Applicants provide evidence of unexpected results of the claimed composition to rebut the assertion of a *prima facie* case of obviousness. Applicants argue that the data presented in Tablet 1-4 on pages 34-37 of the instant specification clearly show superior patch properties, when compared to the patch properties for compositions lacking at least one of the claimed components. Applicants' submission of the expert declaration provides supplemental experimental evidence showing the unexpectedly superior results for the patch cohesion property when the weight ratio (A:B) of the content of the styrene-isoprene-styrene block copolymer (A) to 2-ethylhexyl acrylate - vinyl acetate copolymer (B) is from 1:1 to 9:1. Applicant argues that the Examiner did not comment on the unexpectedly superior skin permeation rates of the patch formulation of the presently pending claims. Applicant argues that there is no teaching or suggestion in the cited combination of references that one of ordinary skill in the art would have had a reasonable expectation of successfully combining the teachings of Miranda et al. with the teachings of Hoffman et al. to devise the claimed unexpectedly superior patch.

This is not persuasive because the combination of Miranda and Hoffman renders limitations of the patch formulation obvious and therefore, the results presented by Applicant are not unexpected. One of ordinary skill in the art would find the adhesive nature of the combination of Miranda and Hoffman obvious and expected since both references teach polymers for the same purpose, i.e., adhesion and cohesion. Please see MPEP 2141.

Therefore, the rejection of 03/18/09 is maintained.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4 and 6 **remain** provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-11 of copending Application No. 10/526,065 (the '065 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a patch comprising a backing layer and an adhesive layer that is compounded with a drug and an adhesive base agent. The adhesive base agent comprises styrene-isoprene-styrene block copolymer, 2-ethylhexyl acrylate-vinyl acetate copolymer and a basic nitrogen-including polymer, which is selected from methyl acrylate-butyl methacrylate-dimethylaminoethyl methacrylate and polyvinyl acetal diethylamino acetate. The drug is selected from a group containing pergolide. The

adhesive layer also comprises an organic acid and an alicyclic saturated hydrocarbon-based tackifier.

Claims 1 and 3-11 of the '065 application are also drawn to a patch comprising a backing layer and an adhesive layer compounded with an adhesive base agent and pergolide. The adhesive base agent comprises an acrylic polymer, a basic nitrogen-including polymer selected from methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer and polyvinyl acetal diethylamino acetate. The adhesive layer also comprises an alicyclic saturated hydrocarbon resin-based tackifier. 2-ethylhexyl acrylate-vinyl acetate copolymer is claimed as an acrylic polymer and styrene-isoprene-styrene block copolymer is claimed as the rubber polymer. The adhesive layer also contains an organic acid (acetic acid and/or a pharmaceutically acceptable salt).

The difference between the instant claims and those of '065 is that claims of '065 include the limitation of the weight ratio of the content of the acrylic polymer to the content of the rubber polymer and the weight ratio of the content of the acrylic polymer and the rubber polymer to the content of the basic nitrogen-including polymer. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the ratio of the content of the acrylic polymer to the content of the rubber polymer and the weight ratio of the content of the acrylic polymer and the rubber polymer to the content of the basic nitrogen-including polymer during the process of routine experimentation in order to achieve optimal skin absorption of the drug.

The instant claims are obvious over the claims of '065 and thus they are not patentably distinct over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

10. Applicant's arguments, see Page 12, filed 07/17/09, with respect to the provisional rejection of claims 1 and 4-6 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-11 of copending Application No. 10/526,065 have been fully considered but are not persuasive.

Applicant argues that claims 1 and 3-11 of co-pending application no. 10/526,065 do not recite the specific combination of components in the adhesive layer that are required by pending claims 1, 4 and 6 of the instant application and that present claims 1, 4, and 6 are patentably distinct from claims 1 and 3-11 of co-pending application no. 10/526,065.

This is not persuasive because the difference between instant claims and those of the '065 Application is that claims of the '065 Application include the limitation of the weight ratio of the content of the acrylic polymer to the content of the rubber polymer and the weight ratio of the content of the acrylic polymer and the rubber polymer to the content of the basic nitrogen- including polymer. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the ratio of the content of the acrylic polymer to the content of the rubber polymer and the weight ratio of the content of the acrylic polymer and the rubber polymer to the content of the

basic nitrogen-including polymer during the process of routine experimentation in order to achieve optimal skin absorption of the drug. The instant claims are obvious over the claims of the '065 Application and thus they are not patentably distinct over each other.

Applicants respectfully request that the Examiner hold this rejection in abeyance until such time as the Examiner indicates there is successful resolution of the claim rejections noted above. Applicants, at that time, will either address the rejection or cancel any conflicting claims in copending U.S. Patent Application No. 10/526,065.

Until such time that there is successful resolution of the claim rejections in the instant application, the provisional rejection of 03/18/09 will be maintained.

Conclusion

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615